UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,408	01/05/2007	Patrick Bosche	BHC 031062	2342

71285 7590 03/05/2009
BAYER HEALTHCARE LLC
P.O.BOX 390
SHAWNEE MISSION, KS 66201

EXAMINER	
HOLT, ANDRIAE M	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
03/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,408	BOSCHE ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :4/18/2006, 4/29/2008, 12/11,2008.

DETAILED ACTION

Claims 1-4 are pending in the application.

Priority

This application is a national stage entry for PCT/EP04/12327 filed October 30, 2004, which claims priority to German Foreign Application No. 103 51 448.1 filed on November 4, 2003.

Information Disclosure Statement

Receipt of Information Disclosure Statements filed on April 18, 2006, April 29, 2008 and December 11, 2008 is acknowledged.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Ursua et al. (EP 1,177,788).

Ursua et al. disclose a pharmaceutical composition of fluoxetin in coated dispersible tablets and the process for its manufacture (Abstract). Ursua et al. disclose in example 1, page 6, a formulation that comprises colloidal silicon dioxide (Aerosil 200) 4 mg, which is 1.51% of the formulation (colloidal silicon dioxide 1.5% by wt.), mint flavour 90351-51 (flavour), and fluoxetin hydrochloride (pharmaceutical ingredient).

Ursua et al. disclose on page 5, paragraphs 29-40, the process for preparing the formulations. Ursua et al. disclose all of the components of the formulation are sieved through a 0.6 mm mesh sieve.

Ursua et al. meet all of the limitations of the claims and thereby anticipate the claims.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al. (US 5,256,699).

Murphy et al. disclose in example 3, col. 2, lines 65-68-col. 4, lines 1-20, that diclofenac free acid (pharmaceutical ingredient) is dry blended with microcrystalline cellulose, sodium crosscarmellose and coloring material. The mass is then wet granulated with water. Murphy et al. disclose the granules are then blended with the remainder of the excipients and compressed into tablets having the following composition comprising: Diclofenac 46.5 (pharmaceutical ingredient); Blackcurrant Flavour 30.0 (flavour); and Colloidal silicon dioxide 4.4, which is 1.5% of the formulation (colloidal silicon dioxide 1.5% by wt).

Murphy et al. meet all of the limitations of the claims and thereby anticipate the claims.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Wadhwa (US 2003/0170310).

Wadhwa discloses a tasteless, granular, directly compressible, stable, fast-dissolving complex of a bitter tasting basic drug, pharmaceutical formulations comprising the tasteless complex of the basic drug and dosage forms thereof are disclosed (Abstract). Wadhwa discloses in example 1 the preparation of Fexofenadine orally disintegrating/mouth dissolving tablet where the ingredients for the 60 mg tablet comprise: fexofenadine-carbomer complex (pharmaceutical ingredient); Flavor - Mixed Fruit (flavour), and Aerosil (Colloidal silicon dioxide) (colloidal silicon dioxide) (page 5, paragraphs 51-52-page 6, paragraph 52). Wadhwa discloses the process for preparing the formulations in paragraphs 53-54 on page 6. Wadhwa discloses lubricants (talc, magnesium stearate, colloidal silicon dioxide, glyceryl behenate, and glyceryl palmitostearate) were mixed separately with aspartame, crosscarmellose sodium and then flavor after sifting each of them through a 60# mesh. Applicant use open terminology, comprising, which opens the formulation to the addition of other components.

Wadhwa meets all of the limitations of the claims and thereby anticipates the claims.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Lech et al. (US 5,681,577).

Lech et al. disclose an improved chewable cold/sinus medication comprising a decongestant pseudoephedrine, and an antihistamine, such as chlorpheniramine maleate or diphenhydramine hydrochloride. Lech et al. disclose the drugs are

incorporated onto an adsorbent material comprising silicon dioxide which surprisingly masks their bitter metallic taste and numbing mouth feel that would otherwise prohibit their use in a chewable tablet dosage form (col. 2, lines 45-52). Lech et al. disclose in example III, col. 5, lines 47-64, the preparation of a chewable cold/sinus child's formulation. Lech et al. disclose the formulation comprises: diphenhydramine HCl (pharmaceutical ingredient); pseudoephedrine HCl (pharmaceutical ingredient); Cab-o-sil® M5 (colloidal silicon dioxide); and grape flavor (flavour). Lech et al. disclose the preparation of the formulation in col. 5, lines 66-67-col. 6, lines 1-22). Applicant use open terminology, comprising, which opens the formulation to the addition of other components.

Lech meets all of the limitations of the claim and thereby anticipates the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2 and 4 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Fekete et al. (WO 01/12162) in view of Vetter et al. (US 5,808,076).

Applicant's Invention

Applicant claims a solid pharmaceutical formulation comprising an active pharmaceutical ingredient, flavoring and at least 1.5% by weight of colloidal silicon dioxide. Applicant claims the active pharmaceutical ingredient is enrofloxacin.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Fekete et al. teach pharmaceutical compositions containing ciprofloxacin, a binder, disintegrating agent and other auxiliary agents (Abstract). Feteke et al. teach the compositions comprise 60-80% by weight of ciprofloxacin (pharmaceutical ingredient), 2-10 % by weight of maltodextrin (flavor), 5-15% by weight of a disintegrating agent of carboxy methyl starch type, and 3-6% by weight of silicon dioxide (silicon dioxide) (page 3-page 4, Description of the invention). Fekete et al. teach on page 16, in Table VIII, the ingredients of the formulations. Fekete et al. teach on page 11, the process of preparation of the pharmaceutical compositions the ingredients are mixed and granulated under the addition of water, drying, homogenizing with 1-3% by weight of a lubricant and pressed into tablets.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Fekete et al. do not teach the pharmaceutical ingredient is enrofloxacin or that the colloidal silicon dioxide is at least 1.5 % by weight of the formulation. It is for this reason Vetter et al. is joined as a secondary reference.

Vetter et al. teach orally administrable formulations of quinolone- or naphthyridonecarboxylic acids by mixing quinolone- or naphthyridonecarboxylic acids with embonic acid in the presence of an excipient, optionally in the presence of auxiliaries, when using dry mixtures in the presence of water.

Vetter et al. teach preferred compounds are: temafloxacin, tosufloxacin, enrofloxacin, ciprofoxacin, ofloxacin, orbifloxacin, marbofloxacin, norfloxacin, benofloxacin, binfloxacin, danofloxacin, difloxacin, sarafloxacin, premafloxacin, and ibafloxacin. Vetter et al. teach in examples 2 and 3, col. 6, lines 40-66, formulations comprising enrofloxacin granules and colloidal silica. Vetter et al. teach other organic substances, such as sugar and other auxiliaries can be added to the formulations.

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Fekete et al. and Vetter et al. and use enrofloxacin as the pharmaceutical ingredient. Fekete et al. teach formulations comprising ciprofloxacin, a flavoring, and silicon dioxide. One skilled in the art at the time the invention was made would have been motivated to use enrofloxacin as the pharmaceutical ingredient because Vetter et al. teach that ciprofloxacin and

enrofloxacin are preferred quinolone compounds. Therefore, the skilled artisan would have be motivated to use enrofloxacin as the pharmaceutical ingredient with a reasonable expectation of success as ciprofloxacin and enorfloxacin have very similar chemical structures, an amine base with a carboxylic acid, and are taught by Vetter et al. to be functional equivalent quinolone compounds.

In reference to the teaching that the colloidal silicon dioxide is at least 1.5 % by weight of the formulation, one skilled in the art at the time the invention was made would have been motivated to use the various weigh ranges as routine experimentation to optimize the results of the formulation. The adjustment of particular conventional working conditions (e.g., determining result effective amounts of the ingredients, such as the weight ratios, beneficially taught by the cited references), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

Claims 1-4 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Fekete et al. (WO 01/12162) in view of Vetter et al. (US 5,808,076) and Daube et al. (DE 10224086).

Applicant's Invention

Applicant claims a solid pharmaceutical formulation comprising an active pharmaceutical ingredient, flavoring and at least 1.5% by weight of colloidal silicon dioxide. Applicant claims the active pharmaceutical ingredient is pradofloxacin.

Determination of the scope of the content of the prior art (MPEP 2141.01)

The teachings of Fekete et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Fekete et al. do not teach the pharmaceutical ingredient is pradofloxacin. It is for this reason Vetter et al. and Daube et al. are joined as secondary references.

The teachings of Vetter et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Daube et al. teach the preparation for oral administration of quinolone antibiotics pradofloxacin or enrofloxacin; the ion exchangers known to mask the bitter taste of the quinolone antibiotics. Daube et al. teach the preparations are administered to animals.

Finding of prima facie obviousness Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Fekete et al., Vetter et al. and Daube et al. and use pradofloxacin as the pharmaceutical ingredient. Fekete et al. teach formulations comprising ciprofloxacin, a flavoring and silicon dioxide. In addition, Vetter et al. teach that ciprofloxacin and enrofloxacin are functional equivalent quinolone compounds. One

skilled in the art at the time the invention was made would have been motivated to use pradofloxacin as the pharmaceutical ingredient because Daube et al. teach that the formulations can be prepared with either pradofloxacin or enrofloxacin. The skilled artisan would have be motivated to use pradofloxacin as the pharmaceutical ingredient with a reasonable expectation of success as ciprofloxacin, enorfloxacin and pradofloxacin have very similar chemical structures, an amine base with a carboxylic acid, and Vetter et al. teach ciprofloxacin and enrofloxacin to be functional equivalent quinolone compounds. Therefore, it would have been obvious to the skilled artisan that pradofloxacin, enrofloxacin and ciprofloxacin would be a functional equivalent quinolone compounds.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

None of the claims are allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is 571-272-9328. The examiner can normally be reached on 9:00 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/John Pak/
Primary Examiner, Art Unit 1616